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SENNIGER POWERS LLP 100 NORTH BROADWAY 17TH FLOOR ST LOUIS, MO 63102			EXAMINER MACAULEY, SHERIDAN R	
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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

uspatents@senniger.com

DETAILED ACTION

A response and amendment were received and entered on July 2, 2008. All evidence and arguments have been fully considered. Claims 42 and 45 have been cancelled. New claims 46-52 have been added. Claims 26-36, 38-41, 43, 44 and 46-52 are pending.

Election/Restrictions

1. Claims 30 and 33-35 have been withdrawn from further consideration due to a previous requirement for restriction. New claims 46, 47 and 50-52 depend from withdrawn claims and are drawn to nonelected species. Claims 30, 33-35, 46, 47 and 50-52 are withdrawn from further consideration due to the aforementioned requirement for restriction. As noted in applicant's arguments, claim 35 was also inadvertently listed among the examined claims. It is noted that claim 35 is withdrawn, as indicated in the previous office action.
2. Claims 26-29, 31, 32, 36, 38-45, 48 and 49, to the extent that they read upon the elected species, are examined on the merits in this office action.

Claim Rejections - 35 USC § 112

3. Rejections under 35 USC 112 have been withdrawn due to amendment.
4. Claims 26-29, 31, 32, 36, 38-45, 48 and 49 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

5. The term "physiological potassium concentration" in claims 26-29 is a relative term which renders the claim indefinite. The term is not defined by the claim, the specification does not provide a standard for ascertaining the requisite degree, and one of ordinary skill in the art would not be reasonably apprised of the scope of the invention. The metes and bounds of the term "physiological potassium concentration" are unclear because applicant has not specified which type of physiology the term refers to (for instance, human, mammalian or another group). Applicant also has not specified whether the "physiological potassium concentration" refers to a normal physiology or an altered physiology, and how one of ordinary skill in the art would be able to ascertain whether or not a concentration is within the specified "physiological potassium concentration."

Claim Rejections - 35 USC § 101

6. Rejections under 35 USC 101 have been withdrawn due to amendment.

Claim Rejections - 35 USC § 103

7. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

8. The factual inquiries set forth in *Graham v. John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

9. Claims 26-29, 31, 32, 35, 36, 38-45 and 48 are rejected under 35 U.S.C. 103(a) as being unpatentable over Chien (US 5,656,420, 1997) in view of Berdyaev et al. (US 5,432,053) and Chien (Journal of Thoracic and Cardiovascular Surgery, 1994, 107:965-967). Claim 26 recites a method for reducing electrical disturbance of a cell's resting membrane potential comprising administering to the cell an effective amount of a composition comprising an effective amount of (i) a local anaesthetic and (ii) an opioid, said composition further comprising a physiological potassium concentration. Claim 27 recites a method for reducing damage to a cell, tissue or organ following ischaemia comprising administering to the cell, tissue or organ an effective amount of a composition comprising an effective amount of a local anaesthetic and an opioid, said composition further comprising a physiological potassium concentration. Claim 28 recites a method for preconditioning a cell or tissue during ischaemia or reperfusion comprising administering an effective amount of a composition comprising an effective amount of a local anaesthetic and an opioid, said composition further comprising a physiological potassium concentration. Claim 29 recites a method for reducing damage to a cell, organ or tissue before, during and following a surgical or clinical intervention

comprising administering to the cell, organ or tissue an effective amount of a composition comprising an effective amount of a local anaesthetic and an opioid, said composition further comprising a physiological potassium concentration. Claims 31 and 32 recite a method according to claim 27 wherein the opioid is selected from enkephalins, endorphins and dynorphins, specifically a delta opioid receptor agonist. Claim 36 recites a method according to claim 27 wherein the cell is a myocyte. Claim 38 recites a method according to claim 27 wherein the composition further comprises ionic magnesium. Claim 39 recites a method according to claim 27 wherein the composition has been oxygenated. Claim 40 recites a method according to claim 27 comprising administering the composition as part of a medicament including the composition and a pharmaceutically acceptable carrier, diluent and/or excipient. Claim 41 recites a method according to claim 40 wherein the medicament has concentrations of one or more of sodium, calcium and chloride lower than physiological concentrations. Claim 43 recites a method according to claim 27 wherein the composition is at a temperature of profound hypothermia (0 to 4 degrees Celsius), moderate hypothermia (5 to 20 degrees Celsius), mild hypothermia (20 to 32 degrees Celsius) or normothermia (32 to 38 degrees Celsius). Claim 44 recites a method according to claim 27 wherein the components of the medicament or composition are combined before administration or when the components are administered substantially simultaneously or co-administered. Claim 45 recites the use of a composition or medicament according to claim 27 for treatment of a subject in need thereof. Claim 48 recites the method of

claim 31 wherein the opioid is an enkephalin which targets delta, alpha and/or mu receptors.

10. Chein (1997) teaches a method for extending the survival time of mammalian lung tissue comprising administering to the tissue a composition comprising an opioid, DADLE, which is an enkephalin and a delta opioid receptor agonist (abstract). Chein (1997) teaches that organ preservation solutions may comprise ionic magnesium (see table in col. 6-7). Chein (1997) teaches that, during perfusion, the preserved tissue and solution was ventilated (i.e. exposed to oxygen, col. 4, lines 64-67). The composition used by Chein (1997) comprises concentrations of ions which are similar to that of a blood-based solution, and contains no calcium, thus the calcium concentration has been adjusted from and is lower than physiological concentrations (col. 7-8). The composition used by Chein (1997) is at a temperature of profound hypothermia and the components are combined before administration (abstract, col. 4, lines 13-40). The teachings of Chein (1997) are directed to the treatment of a subject in need of the treatment (col. 2, line 45-col. 3, line 21). Chein (1997) does not teach that the composition comprises an anesthetic or that the cells which are treated are myocytes.

11. Berdyaev teaches a method for preservation of living tissues by the use of a solution comprising an anesthetic (col. 1, line 60-col. 2, line 38). Berdyaev teaches that the composition is suitable for the preservation of heart tissue, which comprises myocytes (see col. 3, example 1).

12. Chien (1994) teaches that compositions comprising DADLE are suitable for preservation of many different types of tissues, including heart tissues (p. 965, col. 2-p. 966, col. 2).

13. At the time of the invention, a method for the preservation of tissues or cells comprising nearly all of the claimed elements was known, as taught by Chien (1997). Further, methods were known at the time of the invention for using similar compositions to preserve heart tissue and that such compositions could comprise an anesthetic, as taught by Chien (1994) and Berdyaev, respectively. Motivation to combine these teachings is provided by Berdyaev, who teaches that anesthetics are desirable additions to such compositions because they are useful for stabilization of membranes (col. 2, lines 28-30). Further, one would have been motivated to use the method of Chein (1997) for the preservation of tissues other than lung tissue, including heart tissues, because Chein (1994) teaches that compositions comprising DADLE could be used for the preservation of such tissues. The combined method of the cited references would inherently perform all of the functions recited in claims 26-29 because it comprises the claimed method step, i.e. administration of an effective amount the composition recited in the claims. One of ordinary skill in the art would have had a reasonable expectation of success in combining these teachings because all of the teachings are directed to the preservation of the claimed tissues, and thus all of the components in the compositions are suitable for such methods. Therefore, one of ordinary skill in the art would have had a reasonable expectation of success in combining the teachings discussed above to arrive at the claimed invention.

14. Claims 26-29, 31, 32, 36, 38-45, 48 and 49 are rejected under 35 U.S.C. 103(a) as being unpatentable over Chien (US 5,656,420, 1997) in view of Berdyaev et al. (US 5,432,053) and Su (J. Biomed. Sci., 2000, 7:195-199). Claims 26-29, 31, 32, 36, 38-45 and 48 have been discussed above. Claim 49 recites the method of claim 31 wherein the opioid is DPDPE.

15. Chein (1997) teaches a method for extending the survival time of mammalian lung tissue comprising administering to the tissue a composition comprising an opioid, DADLE, which is an enkephalin and a delta opioid receptor agonist (abstract). Chein (1997) teaches that organ preservation solutions may comprise ionic magnesium (see table in col. 6-7). Chein (1997) teaches that, during perfusion, the preserved tissue and solution was ventilated (i.e. exposed to oxygen, col. 4, lines 64-67). The composition used by Chein (1997) comprises concentrations of ions which are similar to that of a blood-based solution, and contains no calcium, thus the calcium concentration has been adjusted from and is lower than physiological concentrations (col. 7-8). The composition used by Chein (1997) is at a temperature of profound hypothermia and the components are combined before administration (abstract, col. 4, lines 13-40). The teachings of Chein (1997) are directed to the treatment of a subject in need of the treatment (col. 2, line 45-col. 3, line 21). Chein (1997) does not teach that the composition comprises an anesthetic or that the cells which are treated are myocytes.

16. Berdyaev teaches a method for preservation of living tissues by the use of a solution comprising an anesthetic (col. 1, line 60-col. 2, line 38). Berdyaev teaches that

the composition is suitable for the preservation of heart tissue, which comprises myocytes (see col. 3, example 1).

17. Su teaches that compositions comprising DADLE are suitable for preservation of many different types of tissues, including heart tissues (p. 196, col. 2, par. 3-p. 197, col. 1, par. 1). Su also teaches that other delta opiod receptor agonists may be used for organ preservation, and that DPDPE provides protective effects in organ preservation (abstract, p. 197, col. 1, par. 4).

18. At the time of the invention, a method for the preservation of tissues or cells comprising nearly all of the claimed elements was known, as taught by Chien (1997). Further, methods were known at the time of the invention for using similar compositions to preserve heart tissue and that such compositions could comprise an anesthetic, as taught by Su and Berdyaev. Motivation to combine these teachings is provided by Berdyaev, who teaches that anesthetics are desirable additions to such compositions because they are useful for stabilization of membranes (col. 2, lines 28-30). Further, one would have been motivated to use the method of Chein (1997) for the preservation of tissues other than lung tissue, including heart tissues, because Su teaches that compositions comprising DADLE and DPDPE could be used for the preservation of such tissues. The combined method of the cited references would inherently perform all of the functions recited in claims 26-29 because it comprises the claimed method step, i.e. administration of an effective amount the composition recited in the claims. One of ordinary skill in the art would have had a reasonable expectation of success in combining these teachings because all of the teachings are directed to the preservation

of the claimed tissues, and thus all of the components in the compositions are suitable for such methods. Therefore, one of ordinary skill in the art would have had a reasonable expectation of success in combining the teachings discussed above to arrive at the claimed invention.

19. Thus, the claimed invention as a whole was *prima facie* obvious over the combined teachings of the prior art.

Response to Arguments

20. Applicant's arguments filed July 2, 2008 have been fully considered but they are not persuasive. Applicant argues that the cited teachings do not render the claimed invention obvious because they fail to teach a method of using a composition comprising a physiological potassium concentration. In response to applicant's argument that the references fail to show certain features of applicant's invention, it is noted that the features upon which applicant relies (i.e., the use of a composition containing a specific phosphate concentration) are not recited in the rejected claim(s). Although the claims are interpreted in light of the specification, limitations from the specification are not read into the claims. See *In re Van Geuns*, 988 F.2d 1181, 26 USPQ2d 1057 (Fed. Cir. 1993). Although applicant argues that the cited references teach the use of a composition with a phosphate concentration above "physiological" levels, applicant has provided no guidance directing one of ordinary skill in the art to ascertain what "physiological" levels applicant refers to and what specific concentration

would be within the metes and bounds of the claims. Thus, the cited teachings, which teach the use of a specific phosphate concentration that can be used physiologically, render the claimed invention obvious. Applicant's arguments have therefore been fully considered but they have not been found to be persuasive.

Conclusion

No claims are allowed.

21. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire **THREE MONTHS** from the mailing date of this action. In the event a first reply is filed within **TWO MONTHS** of the mailing date of this final action and the advisory action is not mailed until after the end of the **THREE-MONTH** shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than **SIX MONTHS** from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to SHERIDAN R. MACAULEY whose telephone number is

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(571)270-3056. The examiner can normally be reached on Mon-Thurs, 7:30AM-5:00PM EST, alternate Fridays.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Michael Wityshyn can be reached on (571) 272-0926. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

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SRM

/Ruth A. Davis/
Primary Examiner, Art Unit 1651